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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,135	02/17/2006	Stephen J. Brand	24492-010 Natl	6830

30623 7590 05/06/2008

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EXAMINER	
CHANDRA, GYAN	
ART UNIT	**PAPER NUMBER**
1646	
MAIL DATE	**DELIVERY MODE**
05/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,135	BRAND ET AL.	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59,66,78,84,86,87 and 89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59,66,78,84,86,87 and 89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/27/07; 2/1/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Re: Brand

Date of Priority: 6/7/2002

DETAILED ACTION

Election/Restrictions

Applicant's election of Group 2 (claims 59-64, 66, 69 and 78-90) and species (rapamycin as an agent, and gastrin17 as a ligand for gastrin/CCK receptor) in the reply filed on 3/12/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 59, 66, 78, 84, 86-87, and 89 are pending and under examination.

Information Disclosure Statement

The information disclosure statements (IDSs) filed on 7/27/2007 and 2/1/2008 have been considered. The crossed out references (C134-C136) have not been considered because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

The Examiner suggests that the syntax of claim 59 can be improved by amending the claim to replace "the gastrin is gastrin17Leu15" to "where the gastrin in the gastrin/CCK receptor ligand is gastrin17(leu15)".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Regarding claim 89, the phrase "recent onset", because the specification does not define what time line would be considered as recent onset of diabetes, the term would vary depending on the time of diagnosis which would not necessarily be indicative diabetes onset. Therefore, for the purpose of comparing the claims with the prior art, it is noted that “recent onset of diabetes” is being interpreted as “any time when diabetes is diagnosed.”

Claims 59, 66, 78, 84, 86-87, and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al (IDS, Diabetologia, February 2002, 45: 224-230) in view of Nardi et al (Presented in IDS of 7/27/07, US Patent No. 5,885,956).

The instant claims are broadly drawn to a pharmaceutical composition comprising an agent suppressing an immune response and a gastrin/CCK receptor ligand, wherein the agent is a rapamycin and the gastrin is gastrin17(Leu15) (claim 59), the composition further comprises tacrolimus (also known as FK506) (claim 66), and a method of treating a diabetic subject comprising administering to said subject a composition comprising rapamycin and gastrin17Leu15 (claim78), wherein said composition comprises gastrin17Leu15, rapamycin and Tacrolimus (claim 84), wherein in said agent which increases islet neogenesis and said agent which suppresses an immune response are administered sequentially (claim 86), wherein said subject is a human (claim 87), and wherein the diabetic subject has recent onset of diabetes (claim 89).

Shapiro et al teach that diabetes mellitus is considered as an autoimmune diseases, which develops as a result of the selective destruction of pancreatic islet beta cells by autuimmune process (page 224, left column). They teach that variety of therapies that delete, suppress or modulate functions of immune system cells and can prevent the destruction of beta cell would be beneficial for treating diabetes (page 224, right column). They teach that patients (human subjects) receiving immunosuppressive drugs (e.g., cyclosporin) experience longer duration of remissions than control patients (page 224 through page 225, line 1). They teach that cyclosporin (which is widely used) is more toxic and suggest using a low dosage of the combination of tarcolimus (FK506) and rapamycin provides synergistic response (page 225, left column, 2nd paragraph). The prior art of record teaches a composition comprising rapamycin and tacrolimus to treat diabetic patients.

Shapiro et al do not teach administering gastrin17(Leu15) with said immunosuppressive agents, and Shapiro et al do not teach that gastrin17(leu15) increases islet neogenesis.

Nardi et al do teach that gastrin/CCK receptor ligands encompass various forms of gastrin such as gastrin34 (big gastrin), gastrin 17 (little gastrin, which is also known as gastrin17(Leu15), or gastrin 8 (mini gastrin), and various forms of cholecystokinin as CCK8, CCK12, CCK22, CCK32 and CCK58. Nardi et al teach that gastrin plays role in the development of pancreatic islet (column 1, lines45+). Nardi et al contemplate using a composition comprising gastrin/CCK receptor ligand for treating diabetes mellitus (claims 1-4, 6-8). Nardi et al teach that the amount of therapeutic, formulations, route of

administration and a combination with other agents can be determined by standard clinical techniques (column 5, lines 60-67 to column 6, lines 1-67).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use gastrin17Leu15 in combination with immunosuppressive agents tacrolimus and rapamycin to treat diabetes as taught by Nardi et al. One would have been motivated to do so because Nardi et al teach using gastrin17 for treating diabetes and Shapiro et al also teach a combination of immunosuppressive agents tacrolimus and rapamycin for treating the same disease. Further, one would have a reasonable expectation of success in using gastin17(Leu15); and tacrolimus (FK506) and rapamycin for treating diabetes because both therapies have been effective in treating diabetes mellitus in patients.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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19 April, 2008
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/Robert Landsman/
Primary Examiner, Art Unit 1647